TABLE 3

Transcripts	Sequence
Substrates	
SP1.1	$_{1}$GGGCGGGUCGG$_{11}$ (SEQ ID: 9)
SG7A	GGGCGGAUCGG (SEQ ID: 15)
SG7C	GGGCGGCUCGG (SEQ ID: 23)
SG7U	GGGCGGUUCGG (SEQ ID: 16)
SU8A	GGGCGGGACGG (SEQ ID: 24)
SU8C	GGGCGGGCCGG (SEQ ID: 17)
SU8G	GGGCGGGGCGG (SEQ ID: 18)
SU8G-9mers	$_{1}$GCGGGGCGG$_{9}$
Ribozymes	
δRzP1.1	$_{20}$CCGACCU$_{26}$
δRzP1-A23C	CCGCCCU
δRzP1-A23G	CCGGCCU
δRzP1-A23U	CCGUCCU
δRzP1-C24A	CCGAACU
δRzP1-C24G	CCGAGCU
δRzP1-C24U	CCGAUCU

Replace the paragraph beginning at page ~~31~~, line ~~31~~ with the following re-written paragraph:

The infuence of 2'-OH groups in RzB on the catalytic activity of RzA:RzB complex was analyzed. 0.066 uM of a mix of cold and end-labeled RNA substrates were incubated in presence of 0.066 uM of RzA and 0.2 uM of various RzB RNA/DNA mixed polymers. The incubation was performed in 50 uM Tris-HCl pH 8.0 and 50 mM $MgCl_2$ at 37°C. An aliquot was removed after one hour and the reaction stopped by the addition of an excess of stop solution (xc, bb, formamide). Reaction mixtures were fractioned on 20% polyacrylamide gel electrophoresis and were exposed on x-ray films. Fully deoxyribonucleotide RzB molecules are not able to support a cleavage activity. Individual deoxy substitution mutants were subjected to catalytic cleavage. All of the reconstituted complexes were active to different extents. S and P respectively represent substrate and product species. As an example, dGg stands for

GGCGCAUGgCUAAGGGACCC (SEQ ID: 55) where uppercase and lowercase letters respectively represent ribo- and deoxyribonucleotides. The results are shown in Figure 6 and Table 7.

Replace the paragraph beginning at page 32, line 14 with the following re-written paragraph:

Table 7 shows the quantification of time course experiments performed. Rate and extent of cleavage values were obtained from fitting the experimental data to the equation $A_t = A_{alpha}$ (1-e-kt) where A_t is the percentage of cleavage at time, t, A_{alpha} is the maximum cleavage and k is the reaction rate. Data analysis was performed with GraFit Version 3.01 from Erithacus Software.

Replace the paragraph beginning at page 33, line 6 with the following re-written paragraph:

Example 7: Cleavage of HDAg mRNA.

Plasmids encoding the HDAg mRNA and delta ribozymes. The pKSAgS plasmid carries the S-HDAg mRNA in pBluescript KS+ (Stratagene). Briefly, the S-HDAg mRNA insert (positions 900 to 1679 of the vHDV.5 variant (according to Lafontaine, D., Mercure, S. and Perreault, J.-P. (1997) Nucleic Acids Res., **25**, 123-125) were retrieved by PCR amplification using pSVL(AgS) (Chao, M., Hsieh, S.Y. and Taylor, J. (1990) J. Virol., **64**, 5066-5069) as template. The oligonucleotides used in this PCR had restriction sites situated at their 5' ends so as to facilitate subsequent cloning: HDV1679.66: 5'CCGGATCCCTCGGGCTCGGGCG 3' (SEQ ID: 41) (underlined is the Bam H1 restriction site) and HDV900.914: 5'CCAAGCTTCGAAGAGGAAAGAAG 3' (SEQ ID: 42) (underlined is the Hind III restriction site). Plasmid DNA (pSVL(AgS), 50 ng), 0.4 mM of each oligonucleotide, 200 mM dNTPs, 1.25 mM $MgCl_2$, 10 mM Tris-HCl pH 8.3, 50 mM KCl, and 1 U Taq DNA polymerase were mixed together in a final volume of 100 µL. The Applicant performed one low stringent PCR cycle (94°C for 5 min, 53°C for 30 s, 72°C for 1 min), followed by 35 cycles at higher stringency (94°C for 1 min, 62°C for 30 s, 72°C for 1 min). The mixture was fractionated by electrophoresis in a 1% agarose gel in 1X TBE buffer (90 mM Tris-borate, 2 mM EDTA pH 8.0), the expected band excised and eluted using the QIAquick gel extraction kit

(Qiagen), and finally digested and ligated into pBluescript KS+. The strategy used for the construction of plasmids carrying ribozymes with modified substrate recognition domains is described above. All constructs were verified by DNA sequencing.

Replace the paragraph beginning at page 34, line 28 with the following re-written paragraph:

In vitro cleavage assays and kinetic analyses. Cleavage assays were performed at 37°C under single turnover conditions with either randomly labelled mRNA (~ 10 nM) or 5'-end labelled small substrates (<lnM), and an excess of ribozyme (2,5 µM) in a 10 µL final volume containing 50 mM Tris-HCl pH 8.0 and 10 mM $MgCl_2$. A pre-incubation of 5 min at 37°C preceeded the addition of the Tris-magnesium buffer which initiates the reaction. After an incubation of 1 to 3 hrs at 37°C, stop-solution (5 µl) was added and the mixture quickly stored at -20°C until its fractionation on 5% denaturing PAGE gels and subsequent autoradiography. Cleavage sites of the active ribozymes were verified by primer extension assays as described previously (Côté, F. and Perreault, J.-P. (1997) J. Mol. Biol., **273**, 533-543). Briefly, oligonucleotides were synthesized to have complementary sequence to positions downstream (~ 100 positions) from the cleavage site according to the mRNA. For example, for the cleavage site of Rz-12, the oligonucleotide primer, 5'CTTTGATGTTCCCCAGCCAGG-3' (SEQ ID: 56) (21mer), was used in the reverse transcriptase reaction containing the ribozyme cleavage reaction mixture.

Replace the title of Table 8 (cont'd) on page 37 with the following re-written title:

mRNA sequence (SEQ ID: 43)

IN THE DRAWINGS

Pursuant to Section 37 C.F.R. 1.85, amended to drawings, showing the proposed changes in red, are submitted herewith for approval on a separate paper addressed to the attention of the Official Draftsperson.

REMARKS

In response to the Office communication dated November 4, 2002, Applicant has amended pages 22, 32, 33 and 35. Page 37 was also similarly amended. Pages 36 and 39